REMARKS

Amendments to the Claims

Claims 16-19 are pending in the application. Claims 16, 18, and 19 are withdrawn from consideration. Claim 17 has been rejected.

Claim 17 has been amended to recite "preventing prothrombotic disorders." Support for this amendment is found on page 41, lines 10-24, in the discussion of decreasing the plasmatic concentration of fibrinogen, but maintaining the coagulation capacity of the still circulating fibrinogen, "avoiding severe vascular thrombosis" while preventing a "predisposition for hemorrhagic state."

Claim 17 has also been amended to recite "removes fibrinogen from circulation." Support for this amendment is found on page 16, line 20-28, discussing "withdraw[ing] fibrinogen from circulation, transforming it in[to] fibrin microthrombs."

Claim 18, withdrawn, has been amended to recite "detecting by the thrombin formation . . .". Support for this amendment is found on page 23, lines 13-14.

New claim 20 is drawn to a method for reducing fibrinogen from the blood and recites administering a prothrombin activator comprising the amino acid sequences set forth in SEQ ID NOs: 1, 2, 3, 4, and 5. Support for claim 20 is found on page 16, lines 20-28.

New claim 21 is directed to the dose of the protein administered. Support is found on page 34, lines 17 and 27.

New claim 22 is directed to where the protein is obtained from. Support is found on page 7, lines 12-17.

New claims 23 is drawn to preventing a prothrombotic state in a patient and recites administering a prothrombin activator comprising the amino acid sequences set forth in SEQ ID NOs: 1, 2, 3,

4, and 5. Support for prevention of clot formation is found on page 8, lines 15-21, and page 10, lines 25-29.

New claim 24 is drawn towards when a patient has a disseminated intravascular coagulopathy. Support for "disseminated intravascular coagulation" is found on page 6, line 17. Support for "coagulopathy" is found on page 5, lines 14-18.

New claim 25 is drawn towards a method for treating prothrombotic disorders. Support is found in claim 14's using the prothrombotic activators as treatment.

New claim 26 is drawn towards a method for reducing fibrinogen from the blood. Support is found in claim 14's using the prothrombotic activators as dysfibrinogening agents and on page 16, lines 20-28.

Examiner Interview

Applicants thank the Examiner for speaking with Applicants' representative on August 15, 2008. In the conversation, the Examiner reiterated the statements in her Notice of Non-Compliant Amendment which issued on July 30, 2008.

Review of Office Action and Notice of Non-Compliant

In the Office Action of August 30, 2007, the Examiner rejected claim 17 as not complying with the written description and enablement requirements of 35 U.S.C. §112. The Examiner stated that the originally filed claims and Specification do not support "treating prothrombotic disorders in an individual in need thereof," or "administering at least one amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, and 5 wherein said effective dose prevents blood clot formation." Applicants respectfully traversed both the written description and enablement rejections.

In the response filed February 28, 2008, Applicants cancelled claim 17 and replaced the term "treating prothrombotic disorders in an individual in need thereof" with "preventing severe

vascular thrombosis in a patient." The Examiner stated in her Notice of Non-Compliant Amendment dated July 30, 2008 that "there is no basis [for preventing severe vascular thrombosis in a patient] in original claim 14; page 16, lines 18-28, and/or pages 24-38 for the method and limitations set forth in new claims 20-23." Applicants respectfully present these remarks in response.

Written Description

As discussed above, the Examiner rejected claim 17 as not complying with the written description requirement. Applicants respectfully traverse.

Applicants have now amended claim 17 to recite "preventing prothrombotic disorders in an individual in need thereof." Applicants submit that preventing prothrombotic disorders is supported by the Specification at page 41, lines 10-24, in the discussion of decreasing the plasmatic concentration of fibrinogen, but maintaining the coagulation capacity of the still circulating fibrinogen, "avoiding severe vascular thrombosis" while preventing a "predisposition for hemorrhagic state." Thus, one of skill would understand that Applicants had possession of a method of preventing prothrombotic disorders at the time of filing.

Furthermore, Applicants submit that the Specification supports "administering at least one amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, and 5, wherein said effective dose removes fibrinogen from circulation." Support is found for "removes fibrinogen from circulation" in the Specificaiton at page 16, line 20-28, discussing of "withdraw[ing] fibrinogen from circulation, transforming it in[to] fibrin microthrombs." Support for the amino acid sequences is found on page 15, lines 1-13, describing the sequences. Support for the activity of the purified protein, Lopap, is found in Descriptions 22-26, found on pages 33-39. From the Specification, one of skill would understand that the fragments would have the enzymatic activity of the Lopap protein, based on Description 5, on page 23, and Descriptions 15-16, on page 29. That activity was also confirmed *in vivo.* (See Descriptions 23-24). Thus, one of skill would have recognized that the Applicants were in possession of a method of preventing prothrombotic disorders in an individual in need thereof by administering at least one

amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, 3, 4, and 5, wherein said effective dose removes fibrinogen from circulation. Applicants respectfully request that the Examiner withdraw the rejection.

Enablement

The Examiner rejected claim 17 as not enabled. The Examiner states that "[t]here is no evidence of record nor reason to believe that any of these protein fragments individually or collectively have any biological activity, particularly that required by claim 17. Their size alone would lead one of ordinary skill in the art to doubt that they possessed any biological activity." Applicants respectfully traverse.

The standard for enablement merely requires that from the disclosure one of skill be able to make and use the invention without undue experimentation. Applicants submit that the Specification discloses the activity of the entire Lopap protein (as discussed above). From the Specification, one of skill could determine that the fragments would have the enzymatic activity of the Lopap protein, based on Description 5, on page 23, and Descriptions 15-16, on page 29. Thus, one of skill would be able to make and use the invention without undue experimentation. Applicants respectfully request that the Examiner withdraw the rejection.

Notice of Non-Compliant Amendment

The Examiner states that the claims in the Amendment filed on February 28, 2008, were "not readable on the elected invention because they are directed to a different method of treatment." Applicants respectfully disagree with the Examiner's interpretation of the Restriction Requirement. The Restriction Requirement which Issue March 8, 2007 stated: "Group III, claim(s) 14, drawn to the use of the prothrombin activator in **treatment**" as opposed to the process of purifying the prothrombin activator fraction, the fragments of the prothrombin activator fraction, or use of the prothrombin activator in diagnosis. (Emphasis added). Applicants elected "use of the prothrombin activator in **treatment**." Changing the term from "Utilization of the prothrombin activator of claim 13 . . . using prothrombin activator as a dysfibrinogening agent in prothrombotic state patients" (Claim 14, as filed) to a "method for treating prothrombotic disorders" (Claim 17, February 28, 2008), to a "method for preventing

severe vascular thrombosis" (Claim 20, February 28, 2008) is all still using the prothrombin activator as **treatment**. If the Examiner had wished to limit the scope of the elected invention to a particular treatment, she should have included that in the description of the elected invention.

Thus, while Applicants have amended the claims in an effort to comply with the Examiner's Notice of Non-Compliant Amendment, Applicants are at a loss to determine exactly which treatment, of the possible conditions and patient populations disclosed in the Specification (as discussed above), the Examiner objects to. Applicants also recognize that returning to claim 14, drawn to a "use," is in an improper format, and therefore, have not reproduced claim 14.

Applicants earnestly request consideration and allowance of the claims presented in this paper.

CONCLUSION

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell Reg. No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: September 2, 2008

Respectfully submitted,

By _____ #30,330

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